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IS GENETIC OBESITY A BOON OR BANE?

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ABSTRACT

Obesity is a heritable trait influenced by genetics, epigenetic, and the environment Obesity is a universal epidemic and is devoted to global morbidity and mortality interfered via the improvement of fatty liver disease, type 2 diabetes (T2D), cardiovascular (CVD), and other diseases. It is an aftereffect of an uplifted caloric absorption, an inactive lifestyle, and a genetic, as well as an epigenetic susceptibility Obesity, is a condition that affects human health adversely. Obesity is a common disease caused by multiple factors. It has been reported heredity plays a strong role in obesity development. Because of this complex, multifactorial pattern, diseases and traits such as obesity are called complex genetic traits. There are sequences of variants present in the population that increases or decreases an individual's risk for obesity in their environment. Gene involves in the development of common forms of obesity, thereby identifying pathways that are causal in patients, will guide clinicians and scientists in designing more effective therapies and in identifying high-risk individuals for early intervention. This is inconsistent with the absence of strong signatures of selection at single nucleotide polymorphisms (SNP'S) linked to obesity. Most SNPs are identified by comparing two chromosomes that are common and shared throughout the world: 90% of such SNPs will be seen again at a frequency of at least 1%. Most of these common variants probably have no functional consequence and are essentially the equivalent of genetic dialect or random differences in spelling with no real significance.

KEYWORDS: Body mass index (BMI), Syndromic obesity, Monogenic Forms of Obesity.

INTRODUCTION:
Linkage analysis, genome-wide association studies, and whole-genome sequencing approaches identified numerous genes participating in the onset of severe obesity. Studies have identified variants in several genes that may contribute to weight gain and body fat distribution. The human genome has been linked to the development of obesity when a favorable environment is present. The involvement of genetic factors in the development of obesity is estimated to be 40–70%. Obesity results from a chronic surplus of energy intake which leads to the storage of excessive amounts of triglycerides in adipose tissue The adverse metabolic effects caused by obesity may result in an increased risk of type 2 diabetes, fatty liver disease, hypertension, cardiovascular disease (CVD), and mortality. In the United States, the current prevalence of obesity among adults is about 33%, currently; more than 200 genetic loci are known to influence adiposity traits

HISTORY:
Ancient Greek medicine recognizes obesity as a medical disorder and records that the Ancient Egyptians saw it in the same way. Hippocrates wrote that "Corpulence is not only a disease itself but the harbinger of others". The Indian surgeon Sushruta (6th century BCE) related obesity to diabetes and heart disorders.He recommended physical work to help cure it and its side effects. For most of human history, mankind struggled with food scarcity. In the 17th century, English medical author Tobias Venner is credited with being one of the first to refer to the term as a societal disease in a published English language book ; the objectives related are specified as follows:

1. Genetics related to obesity
2. Genetic Association and Obesity
3. Monogenic, syndrome and polygenic Forms of Obesity
4. Genetic predisposition to obesity

The methods that were used are that all the writings have been collected from various articles from NCBI; literature databases including PubMed. No such method is been applied to the conclusion Reports have been mentioned from the findings and researches of renowned articles.

MAIN FINDINGS:
Obesity is a complex disorder that is determined by genes, environmental factors, and interaction between genes and the environment.. Although the trend of decreased physical activity and increased caloric intake is probably responsible for the recent rise in obesity, it is important to understand that these trends are playing out on a background of genetic variation in the population. Each individual's genetic background remains an important determinant. Pathogenesis of obesity involves multiple interactions among environmental and genetic factors

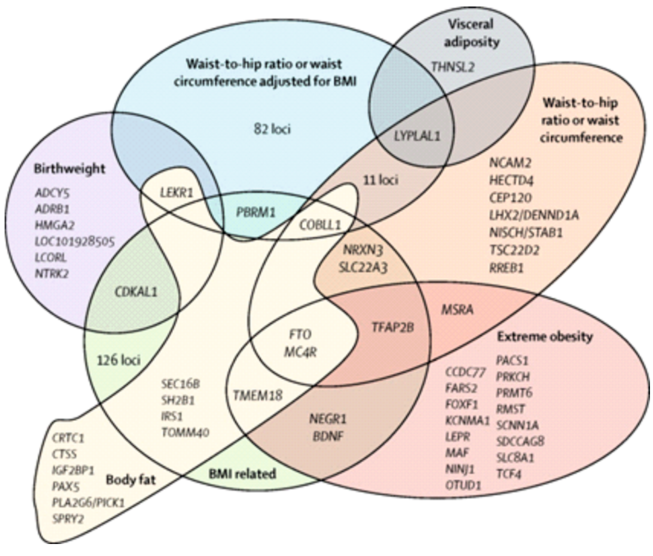

Figure 1: The figure demonstrates the association of gene/s in rising body weight and obesity subsequently.

Heritability:
Quantitative genetics analyses have shown significant heritability, individual chances of being obese are increased when having obese relatives with an estimated heritability of 40-80%. Twin studies have shown a close correlation between the weights of identical twins even when they are reared in dissimilar environments. A recent study suggested that having an obese father and a healthy-weight mother significantly increased the odds of childhood obesity but having an obese mother and a healthy-weight father was not associated with an increased risk of childhood obesity . This discrepancy suggests the role of epigenetic factors in hereditary risk.

Monogenic Forms of Obesity:
Some forms of obesity are caused by single-gene mutations which are rare and severe, following the Mendelian pattern of inheritance which frequently disrupts the leptin-melanocortin pathway.. In humans, obesity cases due to single-gene mutations are reported in 11 different genes including leptin gene, leptin receptor, proopiomelanocortin (POMC), and melanocortin four receptor (MC4R) genes. As of now, obesity due to genetic changes is due to defect in the satiety centers in the brain which affects appetite control centers in the brain

Syndromic obesity:
Rare syndromes caused by discrete genetic defects or chromosomal abnormalities with obesity as a clinical feature associated with mental retardation, dysmorphic features, and organ-specific abnormality. The most frequent of these syndromes is Prader-Willi syndrome which is caused by a chromosomal abnormality of an imprinted region on chromosome 15. Positional genetic strategies have contributed to the identification of several causative mutations. Polygenic obesity is caused by the cumulative contribution of a large number of genes whose effect is amplified in an obesogenic environment.

Genetic Association and Obesity:
The majority of obese individuals occur randomly in the population. It is now accepted that obesity is a complex non-Mendelian trait that might result from numerous susceptible loci. Currently, 135 different candidate genes have been linked with obesity-related phenotypes. Such studies achieved incomplete success in predisposition to obesity risk because these studies are dependent on suspected disease-causing genes derived from a particular biological hypothesis on the pathogenesis of obesity. Genome-Wide Association Studies In context to genetic epidemiology, a genome-wide association study is an evaluation of genetic variants in different individuals to spot if any genetic variant from the whole genome is associated with a certain trait. Genome-Wide Association Studies (GWAS) uses microarray technology to spot associations between specific disease or trait and genetic variants across the entire genome, rather than in a specific gene or locus.

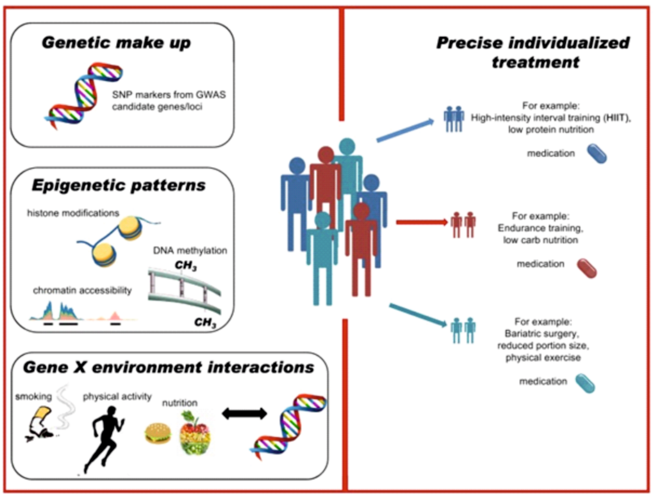

Figure 2: Figure demonstrates the screening process for variations in genes associated in obesity.

This representation of the specific methodology represents the basic view behind GWAS. The DNA samples bind to a microarray chip which is a collection of millions of microscopic.

Genetic predisposition to obesity:
Genetic predisposition to obesity is factually a paradox: The occurrence of obesity in modern societies has two major contributory factors an environmental change that has happened in historical times & a genetic predisposition that has its origins in our history of mankind. Understanding both factors is complex. Three different types have been explained from the evolutionary history of mankind on this globe. Obesity was once adaptive and enabled us to survive through periods of famine. People carrying so-called thrifty genes that enabled the storage of energy as fat between famines would be at a selective advantage. In the modern world, people who have inherited these genes deposit fat in preparation for a famine that never comes. The cause is widespread obesity. The main problem associated with this is why if obesity was historically so advantageous many people did not inherit these thrifty genes and in the modern world are remaining to maintain a slim structure of the body, despite the environmental changes favoring the fat storage? Obesity is not adaptive & may never have existed in our evolutionary past, but it is favored today as an abnormal byproduct of positive selection on some other trait. An example of this explanation can be given by the suggestion that obesity results from variations in Brown Adipose Tissue. Finally, the explanation is that most mutations in the genes that predispose us to obesity are neutral and have been drifting over thrifty genes. As an adaptive response, epigenetic regulation of gene expression may impact the manifestation of genetic predisposition to obesity.

Human obesity has a large genetic component, yet has many serious negative consequences. The idea is that genes predisposing to obesity may have been selected for by repeated exposure to famines. However, this idea has many flaws: for instance, the selection of the supposed magnitude throughout human evolution would fix any thrifty alleles and there is no evidence that hunter-gatherer populations become obese between famines. A thrifty late is that selection in famines that has only happened since the agricultural revolution. Almost 50 years ago, Neel proposed a hypothesis to explain the prevalence of obesity and diabetes in modern society.

In modern society, such genes are disadvantageous because they promote fat deposition in preparation for a famine that never comes, and the result is widespread obesity and diabetes and obese people would be expected to sustain fecundity longer in the face of food shortages. The net effect of famines on fecundity is consequently insufficient to rescue the thrifty gene idea. There are three basic models:

1. The set-point,
2. Settling point and
3. Dual-intervention point models

Hereby, we can conclude that each of the obesity genes likely makes only a a small contribution to body weight, but together inherited variation plays a large role in determining how an individual responds to the environmental factors of diet and physical activity. The obesity epidemic is attributable to dietary and behavioral trends acting on a person's genetic makeup to determine body mass and susceptibility to obesity-related disease. Common forms of obesity have a strong hereditary component yet genetic pathways that contribute to obesity have not been yet discovered. New research tools and large studies will lead to an understanding of genes and their interaction towards that may cause obesity, which may help guide successful interventions and treatments regarding obesity that can be helpful to the upcoming generation with obsessed structures of the human body. With new molecular tools and resources, well-functionalized studies can be undertaken to find common obesity genes in the future. These genes will identify basic and root causes of obesity, potentially suggesting new therapies or Interventions, and provide tools for the understanding of how people respond to their environment to become obese or remain lean.

Obesity-Promoting Genes-Promoting World:
Genes control physiology, development, and adaptation. Obesity is no omission. Little is known about the genes that are devoted to obesity.

"Common Obesity" Caused by Mutations:
Some people have always gravitated to carrying more body fat than others. It is because of susceptibility to obesity, a genetic component.

Research on genes protective against obesity:
Genes also protect against obesity. The GPR75 variants allele's sequenced exomes are protective against obesity. Other anti-obesity-related genes are ALK, TBC1D1, and SRA1.

Gene discovery research:
The access to identify genes associated to obesity bank on the form of obesity and genotyping technology.Unaffected family members were examined for potential gene-disrupting causal mutations via Sanger sequencing.

What do genes have to do with obesity?
Obesity is the outcome of energy shortcoming in a person who invariably takes in more calories from food and drink than are needed to influence their body's metabolic and physical functions. The accelerated population popularity of obesity in recent decades has been attributed to an "obesogenic" environment, which offers ready access to high-calorie foods but limits opportunities for physical activity. The obesity epidemic can be considered a cumulative response to this environment. Obesity is a health problem because it increases the risk of developing diabetes, heart disease, stroke, and other serious diseases.

How do genes control energy balance?
The brain administers food intake signals received from fat tissue, the pancreas, and the digestive tract. These signals are transmitted by leptin, insulin, and ghrelin, and other small molecules. The brain coordinates signals with other

inputs and responds with instructions to the body.

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